



wherein R is methyl or ethyl;

R<sub>1</sub> is chloro or fluoro;

R<sub>2</sub> is hydrogen or fluoro;

R<sub>3</sub> is hydrogen, fluoro, chloro, methyl, ethyl, methoxy or ethoxy;

R<sub>4</sub> is hydrogen or fluoro;

R<sub>5</sub> is chloro, fluoro or trifluoromethyl;

or a pharmaceutically acceptable salt thereof;

or a pharmaceutically acceptable prodrug ester thereof;

in combination with one or more pharmaceutically acceptable carriers.

48. <sup>28</sup> A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 47 <sup>27</sup> comprising an effective cyclooxygenase-2 inhibiting amount, which amount is substantially free of cyclooxygenase-1 activity, of a compound of formula I wherein R is methyl or ethyl; R<sub>1</sub> is chloro or fluoro; R<sub>2</sub> is hydrogen; R<sub>3</sub> is hydrogen, fluoro; chloro or methyl; R<sub>4</sub> is hydrogen; and R<sub>5</sub> is chloro or fluoro; or a pharmaceutically acceptable salt thereof; or a pharmaceutically acceptable prodrug ester thereof; in combination with one or more pharmaceutically acceptable carriers.

49. <sup>29</sup> A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 47 <sup>27</sup> comprising an effective cyclooxygenase-2 inhibiting amount which amount is substantially free of cyclooxygenase-1 inhibiting activity, of a compound of formula I wherein R is methyl or ethyl; R<sub>1</sub> is fluoro; R<sub>2</sub> is hydrogen; R<sub>3</sub> is hydrogen or fluoro; R<sub>4</sub> is hydrogen; and R<sub>5</sub> is chloro; or a pharmaceutically acceptable salt thereof; or a pharmaceutically acceptable prodrug ester thereof; in combination with one or more pharmaceutically acceptable carriers.

50. <sup>30</sup> A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 47 <sup>27</sup> comprising an effective cyclooxygenase-2 inhibiting amount, which amount is substantially free of

cyclooxygenase-1 inhibiting activity, of a compound of formula I wherein R is methyl or ethyl; R<sub>1</sub> is fluoro; R<sub>2</sub> is fluoro; R<sub>3</sub> is hydrogen or ethoxy; R<sub>4</sub> is fluoro; and R<sub>5</sub> is fluoro; or a pharmaceutically acceptable salt thereof; or a pharmaceutically acceptable prodrug ester thereof; in combination with one or more pharmaceutically acceptable carriers.

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51. A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 47/27 comprising an effective cyclooxygenase-2 inhibiting amount which amount is substantially free of cyclooxygenase-1 inhibiting activity, of a compound of formula I wherein R is methyl; R<sub>1</sub> is fluoro; R<sub>2</sub> is hydrogen; R<sub>3</sub> is hydrogen or fluoro; R<sub>4</sub> is hydrogen; and R<sub>5</sub> is chloro; or a pharmaceutically acceptable salt thereof; or a pharmaceutically acceptable prodrug ester thereof; in combination with one or more pharmaceutically acceptable carriers.

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52. A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 47/27 comprising an effective cyclooxygenase-2 inhibiting amount which amount is substantially free of cyclooxygenase-1 inhibiting activity, of a compound of formula I wherein R is methyl or ethyl; R<sub>1</sub> is fluoro; R<sub>2</sub>-R<sub>4</sub> are hydrogen or fluoro; and R<sub>5</sub> is chloro or fluoro; or a pharmaceutically acceptable salt thereof; or a pharmaceutically acceptable prodrug ester thereof; in combination with one or more pharmaceutically acceptable carriers.

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53. A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 47/27 comprising an effective cyclooxygenase-2 inhibiting amount which amount is substantially free of cyclooxygenase-1 inhibiting activity, of 5-methyl-2-(2'-chloro-6'-fluoroanilino)phenylacetic acid of formula I wherein R is methyl; R<sub>1</sub> is fluoro; R<sub>2</sub> is hydrogen; R<sub>3</sub> is hydrogen; R<sub>4</sub> is hydrogen; and R<sub>5</sub> is chloro; or a pharmaceutically acceptable salt thereof; in combination with one or more pharmaceutically acceptable carriers.

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54. A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 47/27 comprising an effective cyclooxygenase-2 inhibiting amount, which amount is substantially free of cyclooxygenase-1 inhibiting activity, of 5-methyl-2-(2',4'-difluoro-6'-chloroanilino)phenylacetic acid of formula I wherein R is methyl; R<sub>1</sub> is fluoro; R<sub>2</sub> is hydrogen; R<sub>3</sub> is fluoro; R<sub>4</sub> is hydrogen; and R<sub>5</sub> is chloro; or a pharmaceutically acceptable salt thereof; in combination with one or more pharmaceutically acceptable carriers.

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55. A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 47/27 comprising an effective cyclooxygenase-2 inhibiting amount, which amount is substantially free of

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cyclooxygenase-1 inhibiting activity, of 5-ethyl-2-(2',3',5',6'-tetrafluoroanilino)phenylacetic acid of formula I wherein R is ethyl; R<sub>1</sub> is fluoro; R<sub>2</sub> is fluoro; R<sub>3</sub> is hydrogen; R<sub>4</sub> is fluoro; and R<sub>5</sub> is fluoro; or a pharmaceutically acceptable salt thereof; in combination with one or more pharmaceutically acceptable carriers.

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56. A selective cyclooxygenase-2 inhibiting pharmaceutical composition according to claim 53 comprising an effective cyclooxygenase-2 inhibiting amount, which amount is substantially free of cyclooxygenase-1 inhibiting activity, of 5-methyl-2-(2'-chloro-6'-fluoroanilino)phenylacetic acid; in combination with one or more pharmaceutically acceptable carriers.

#### REMARKS

Claims 46 to 56 have been added.

Claim 46 has been added to particularly claim the method of use directed to the free acid specified in method of use claim 43.

Claims 47-56 have been added to claim selective cyclooxygenase-2 (COX-2) inhibiting pharmaceutical compositions substantially free of cyclooxygenase-1 (COX-1) inhibiting activity, corresponding in scope of compounds to method of use claims 37-46, respectively. As is the case in previously allowed method of use claims 37-45, the pharmaceutical composition claims specify the effective COX-2 inhibiting amount of the active ingredient to be substantially free of COX-1 inhibiting activity.

The instant pharmaceutical composition claims are supported by the application as filed, e.g. on page 19, par. 1 and 2, and original claims 10-13. New claim 47 replaces cancelled original claim 10, amended so as to correspond in scope to method of use claim 37. New claim 53 replaces cancelled original claim 11. New claim 54 replaces cancelled original claim 12. New claim 55 replaces cancelled original claim 13.

Supporting biological data demonstrating highly selective cyclooxygenase-2 inhibition by active ingredients of the composition claims, e.g. claims 53-56, appears on page 7 (second and third paragraphs from bottom of page) and page 8 (4<sup>th</sup> paragraph).